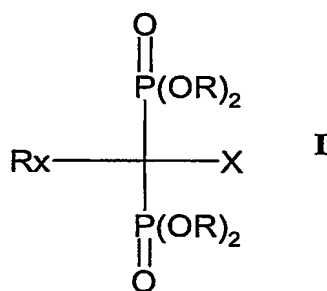


CLAIMS

1. A pharmaceutical preparation for treatment of malignancies, which comprises a chemotherapeutic agent selected from the group consisting of: taxol, a derivative thereof, and aromatase inhibitor and TRAIL; and a bisphosphonate for sequential use.
2. A pharmaceutical preparation according to claim 1 in which the bisphosphonate is an N-bisphosphonate.
3. A pharmaceutical preparation according to claim 1 in which the bisphosphonate is a compound of formula I



wherein

X is hydrogen, hydroxyl, amino, alkanoyl, or an amino group substituted by C₁-C₄ alkyl, or alkanoyl;

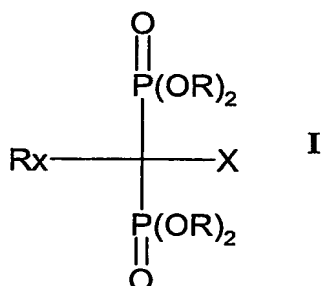
R is hydrogen or C₁-C₄ alkyl and

Rx is a side chain which contains an optionally substituted amino group, or a nitrogen containing heterocycle (including aromatic nitrogen-containing heterocycles), or a pharmaceutically acceptable salt thereof or any hydrate thereof.

4. A pharmaceutical preparation according to claim 1, in which the bisphosphonate is 2-(imidazol-1-yl)-1-hydroxyethane-1,1-diphosphonic acid (zoledronic acid) or a pharmacologically acceptable salt thereof.

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5. A pharmaceutical preparation according to claim 1, in which the chemotherapeutic agent is paclitaxel or letrozole.
6. A pharmaceutical preparation according to claim 1, in which the chemotherapeutic agent is TNF-related apoptosis inducing ligand.
7. A method of treating a patient suffering from a malignant disease comprising administering to the patient an effective amount of a chemotherapeutic agent selected from: taxol or a derivative thereof or letrozole; followed sequentially by an effective amount of a bisphosphonate.
8. A method according to claim 7 wherein the bisphosphonate is an N-bisphosphonate.
9. A method according to claim 7 wherein the bisphosphonate is a compound of formula I



wherein

X is hydrogen, hydroxyl, amino, alkanoyl, or an amino group substituted by C₁-C₄ alkyl, or alkanoyl;

R is hydrogen or C₁-C₄ alkyl and

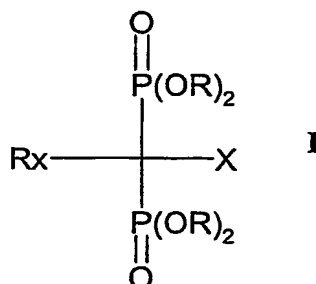
Rx is a side chain which contains an optionally substituted amino group, or a nitrogen containing heterocycle (including aromatic nitrogen-containing heterocycles), or a pharmaceutically acceptable salt thereof or any hydrate thereof.

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10. A method according to claim 7 wherein the bisphosphonate is 2-(imidazol-1-yl)-1-hydroxyethane-1,1-diphosphonic acid (zoledronic acid) or a pharmacologically acceptable salt thereof.
11. A method according to claim 7 wherein the chemotherapeutic agent is paclitaxel.
12. A method according to claim 7 wherein the chemotherapeutic agent is an aromatase inhibitor and is letrozole.
13. A method of treating a patient suffering from a malignant disease comprising administering to the patient an effective amount of a bisphosphonate followed sequentially by an effective amount of TNF-related apoptosis inducing ligand.
14. A method according to claim 13 wherein the bisphosphonate is 2-(imidazol-1-yl)-1-hydroxyethane-1,1-diphosphonic acid (zoledronic acid) or a pharmacologically acceptable salt thereof.
15. The sequential use of a chemotherapeutic agent selected from the group consisting of: taxol, a derivative thereof, an aromatase inhibitor and TRAIL; and a bisphosphonate to inhibit cancer cell growth or induce cancer cell apoptosis.
16. Use according to claim 15 wherein the chemotherapeutic agent is paclitaxel and is delivered prior to the bisphosphonate.
17. Use according to claim 15 wherein the chemotherapeutic agent is letrozole and is delivered prior to the bisphosphonate.
18. Use according to claim 15 wherein the chemotherapeutic agent is TRAIL and is delivered sequentially after the bisphosphonate.

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19. Use of a bisphosphonate in the manufacture of a medicament for the treatment of malignancies in a patient already receiving a chemotherapeutic agent selected from the group consisting of: taxol, a derivative thereof, letrozole and TRAIL.
20. Use of a chemotherapeutic agent selected from the group consisting of: taxol, a derivative thereof, letrozole and TRAIL; in the manufacture of a medicament for the treatment of malignancies in a patient already receiving a bisphosphonate.
21. Use according to claim 18 or 19 wherein the chemotherapeutic agent is selected from the group consisting of: taxol, a derivative thereof and letrozole; and wherein the bisphosphonate is to be administered sequentially after the chemotherapeutic agent.
22. Use according to claim 18 or 19 wherein the chemotherapeutic agent is TRAIL, and wherein the TRAIL is to be administered sequentially after the bisphosphonate.
23. Use according to any one of claims 15 to 22 wherein the bisphosphonate is an N-bisphosphonate.
24. Use according to any one of claims 15 to 22 wherein the bisphosphonate is a compound of formula I



wherein

X is hydrogen, hydroxyl, amino, alkanoyl, or an amino group substituted by C₁-C₄ alkyl, or alkanoyl;

R is hydrogen or C₁-C₄ alkyl and

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Rx is a side chain which contains an optionally substituted amino group, or a nitrogen containing heterocycle (including aromatic nitrogen-containing heterocycles), or a pharmaceutically acceptable salt thereof or any hydrate thereof.

25. Use according to any one of claims 15 to 22 wherein the bisphosphonate is 2-(imidazol-1yl)-1-hydroxyethane-1,1-diphosphonic acid (zoledronic acid) or a pharmacologically acceptable salt thereof.

26. A commercial package comprising a unit dosage form of a bisphosphonate or a pharmaceutically acceptable salt thereof, or any hydrate thereof, and a unit dosage form of a chemotherapeutic agent selected from the group consisting of: taxol, a derivative thereof, an aromatase inhibitor and TRAIL; together with instructions for administering sequential unit doses of said chemotherapeutic agent and said bisphosphonate for the treatment of malignant diseases.